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Health status of Persian Gulf War veterans: self-reported symptoms, environmental exposures and the effect of stress

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Background Most US troops returned home from the Persian Gulf War (PGW) by Spring 1991 and many began reporting increased health symptoms and medical problems soon after. This investigation examines the relationships between several Gulf-service environmental exposures and health symptom reporting, and the role of traumatic psychological stress on the exposure-health symptom relationships.

Methods Stratified, random samples of two cohorts of PGW veterans, from the New England area (n = 220) and from the New Orleans area (n = 71), were selected from larger cohorts being followed longitudinally since arrival home from the Gulf. A group of PGW-era veterans deployed to Germany (n = 50) served as a comparison group. The study protocol included questionnaires, a neuropsychological test battery, an environmental interview, and psychological diagnostic interviews. This report focuses on self-reported health symptoms and exposures of participants who completed a 52-item health symptom checklist and a checklist of environmental exposures.

Results The prevalence of reported symptoms was greater in both Persian Gulf-deployed cohorts compared to the Germany cohort. Analyses of the body-system symptom scores (BSS), weighted to account for sampling design, and adjusted by age, sex, and education, indicated that Persian Gulf-deployed veterans were more likely to report neurological, pulmonary, gastrointestinal, cardiac, dermatological, musculoskeletal, psychological and neuropsychological system symptoms than Germany veterans. Using *a priori* hypotheses about the toxicant effects of exposure to specific toxicants, the relationships between self-reported exposures and body-system symptom groupings were examined through multiple regression analyses, controlling for war-zone exposure and post-traumatic stress disorder (PTSD). Self-reported exposures to pesticides, debris from Scuds, chemical and biological warfare (CBW) agents, and smoke from tent heaters each were significantly related to increased reporting of specific predicted BSS groupings.

Conclusions Veterans deployed to the Persian Gulf have higher self-reported prevalence of health symptoms compared to PGW veterans who were deployed only as far as Germany. Several Gulf-service environmental exposures are associated with increased health symptom reporting involving predicted body-systems, after adjusting for war-zone stressor exposures and PTSD.

Keywords Gulf War veterans, health symptoms, environmental exposures, stress

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Most US troops returned home from the Persian Gulf War (PGW) by Spring 1991 and many began reporting increased health symptoms and medical problems soon after.[1,2] Several explanations have been proposed for the adverse health changes. Two of the most prominent are exposure to environmental hazards while in the Gulf and psychological stress. This investigation examines the relationships between several specific Gulf-service environmental exposures and health symptom reporting, and the role of traumatic psychological stress on the exposure-health outcome relationships. The study approach was not designed to address whether a distinct Gulf War Syndrome exists or can be defined.

Commonly reported physical symptoms by PGW veterans include fatigue, joint pain, headaches, rash and dermatitis, and memory loss.[3–6] Gulf-service environmental exposures capable of producing these reported symptoms include exposure to the neurotoxicants pyridostigmine bromide (anti-nerve gas pills);[7,8] nerve agents[9] such as sarin; pesticides[10] and insect repellents;[11] and exposure to products of combustion found in smoke from oil well fires, smoke from tent heaters, and smoke from burning human wastes.[12,13] The possibility that Iraqis may have deployed chemical warfare agents in the Scud missile attacks exists. Military personnel may also have been exposed to sarin (and other nerve agents) during allied destruction of Iraqi chemical warfare supplies.[14]

In addition, several investigations have demonstrated that severe stress can affect physical well-being in veterans.[15–17] It has been suggested that the 'stress' of exposure to traumatic, wartime events contributes to PGW veterans' health symptoms.[18,19]

Comparisons of the problems of PGW returnees and those of their counterparts in the Vietnam War are inevitable.[18] In many respects, study of the effects of exposures in the Persian Gulf conflict is even more difficult than for the Vietnam War, as few accessible and useful records exist concerning the many possible exposures, there is currently no known biomarker of exposure comparable to serum dioxin levels for Agent Orange exposure, units travelled rapidly and widely over terrain that varied little, and the haste with which the mobilization and response occurred did not allow maintenance of careful records on the location of personnel.

As with Vietnam veterans, systematic study of PGW veterans did not begin in most cases until some time after complaints became evident. One of the few exceptions to this is a study begun of a representative group of veterans within days of their return to Fort Devens in Massachusetts. This report describes the first results from studies designed to evaluate veterans from this group and a similar group in Louisiana followed from a few months of their return (the New Orleans cohort). We use as a comparison group a unit deployed only as far as Germany at the time of the Gulf War. The study is important as it represents one of the first to examine a sample of PGW veterans followed longitudinally since their return from the Gulf. The combined Devens and New Orleans study samples include people representing all military branches (although with a higher proportion of Army troops); all duty services (National Guard, Reserve, and Active duty); and different unit types (e.g. transportation, medical, engineering, military police) and members with varying occupation codes.

Since longitudinal data are available, some characteristics of subjects who were willing to participate (participation bias) can be examined. The use of a unit activated and deployed to a foreign location other than the Gulf during the time of the PGW as a comparison group rather than a non-deployed group reduces the potential bias of reasons for non-deployment present in other studies. The Germany group also experienced some of the same stress of deployment as the Gulf-deployed group, such as leaving one's job and family for an indeterminate length of time and being sent overseas.

As with other studies of PGW veterans, this paper examines self-reported exposures and symptoms. The current state-of-the-art in studies of PGW veterans' health issues does not yet allow the objective measurement of environmental exposures or of specific signs of the underlying illness. However, it is still possible to narrow the range of possible explanations for self-reported adverse health effects in important ways using the data as they now exist. This is especially important given the urgency of the problem and the large number of possible directions for future research. This paper examines the extent to which the reported symptoms 'make sense' in terms of the expected toxicant effects of reported exposures and whether the stress of mobilization and the war-related experiences is a sufficient explanation for the elevated symptom prevalence of PGW-deployed veterans.

Based on prior research,[7–13] the following hypothesized relationships of Gulf-specific toxicant exposures were explored: (1) self-reported exposure to anti-nerve gas pills and gastrointestinal, musculoskeletal, neurological, neuropsychological, and/or psychological symptoms; (2) self-reported exposures to pesticides and dermatological, gastrointestinal, musculoskeletal neuropsychological, neurological, and/or psychological symptoms; (3) self-reported exposure to debris from Scuds, and chemical and biological warfare (CBW) agents and dermatological, musculoskeletal, neurological, neuropsychological, and/or psychological symptoms; (4) self-reported exposure to oil fire smoke, vehicle exhaust, smoke from tent heaters, and smoke from burning human waste and cardiac, neurological, and/or pulmonary symptoms.

To date, no epidemiological studies have examined the health status of PGW veterans for specific environmental exposure-health outcome relationships, controlling for the effects of traumatic stress, although stress is widely discussed as the explanation for the reported symptoms.[18,19] Several questions are addressed: Do Gulf-deployed veterans report higher rates of health symptoms compared to Germany-deployed veterans? Are relationships observed between reported exposure to Gulf-specific environmental exposures and health symptoms as predicted by *a priori* hypotheses? What effect does traumatic stress (specifically post-traumatic stress disorder, [PTSD]) have on the observed exposure-health symptom relationships?

Methods

Study population

Three cohorts were studied, two of veterans deployed to the Gulf and one of veterans deployed only as far as Germany. The Gulf-deployed veterans of study were selected from larger cohorts via a stratified, random sampling strategy designed to produce an equal representation of higher and lower symptom reporters and to oversample for women. The Germany-deployed cohort was represented by a sample of a National

Guard unit from Maine. An evaluation of possible biases regarding the people who participated in the study is given in Results.

Devens cohort

The larger Devens cohort includes 2949 US Army Active, Reserve, and National Guard veterans followed since their return to the US immediately after the war. An initial survey (Spring 1991) was conducted at Ft Devens, MA, within 5 days of return, before soldiers rejoined their families, and assessed psychological well-being, demographics, and self-reported combat exposure.[20,21] The cohort is largely male (92%), Caucasian (83%), and from the National Guard component (52%). Thus, in some respects, it differs from the troop duty status and ethnic breakdown of the total US Gulf force, which was 17% Reserve and Guard troops, and 68% Caucasian.[22] In Winter 1992/Spring 1993, 2313 of these veterans (78% response rate) completed a follow-up survey designed to assess longer-term self-reported physical and psychological well being.[23] Comparison of respondents and non-respondents for this second survey showed a significantly higher percentage of non-respondents were on active duty (53% versus 21%, $P < 0.001$) and of African-American background (17% versus 6%, $P < 0.001$), but they did not differ in sex or education level.

For this study (Spring 1994–Fall 1996) we selected a stratified, random sample of 353 respondents who completed the Health Symptom Checklist (HSC)[24] from the 1992/1993 survey. Of these, 220 (85% of those who could be located and contacted; 62% of the total) participated in at least one part of the study protocol.

New Orleans cohort

The New Orleans cohort consists of 928 Active, Reserve, and National Guard, US Army, Navy, Marine, and Air Force troops deployed to the Gulf. It has also been followed since its return to this country. An initial survey was conducted within 9 months (on average) of their return in 1991.[25] Similar to the Devens cohort, they were largely male (87%), but had a higher proportion of African-Americans (34%) and included other branches of the service besides Army personnel. The make-up of the New Orleans group also differs to some extent from the overall US PGW troop contingent.

We selected a stratified, random sample of 194 of the initial respondents who completed the HSC, of which 73 (58% of those who could be located and contacted; 38% of those sampled) participated in at least one part of the study protocol between Summer 1994 and Fall 1995. Budgetary constraints prevented continued recruitment of study subjects past September 1995.

Germany-deployed cohort

A unit from an air ambulance company activated and sent overseas to Germany during the PGW (December 1990–August 1991) was recruited as a comparison group. It consisted of medics, helicopter pilots, flight crews, mechanics, communications specialists, and administrative support personnel whose intended mission was the handling and transport of wounded US soldiers evacuated from the Gulf. Due to low US casualties, however, the unit assisted German civilian evacuation and transport missions. Fifty subjects (85% of those who could be located and contacted; 51% of the deployed unit) were tested in the Spring of 1995.

Sampling procedure

The stratified, random samples from the larger Devens (n = 2313; 1992/1993) and New Orleans (n = 928; 1991) cohorts were selected using a scheme designed to give an equal representation of higher and lower symptom reporters. We also oversampled for women so that specific gender-related issues could be addressed.

The stratified sampling for symptom reporting used information collected from the 20-item HSC, in which each subject was asked to report the frequency that he/she experienced symptoms over the past several weeks. Each response was scaled from 0 to 3 (0 = none; 1 = a little; 2 = often; 3 = very often). Any score but zero was considered endorsement of a symptom for sampling purposes.

For both cohorts, we excluded those in units with less than 10 people and people in Special Forces units, the latter because they were Active duty troops and likely to be currently deployed to other locations or otherwise difficult to recontact. In addition, people from the Puerto Rican graves registration unit in the New Orleans cohort were excluded. After exclusions, the Devens cohort included 2021 people (1831 men, 190 women) for whom there were complete HSC data. The New Orleans cohort included 818 people (719 men and 99 women).

High and low symptom units were established as one set of strata. This was done primarily because it was anticipated that any environmental exposure information from the US Army Center for Health Promotion and Preventative Medicine (CHPPM) and US Army Center for Research of Unit Records (RUR) would only be available at the unit level. If >50% of unit members reported >5 health symptoms, then the unit was designated a 'high symptom unit'; if ≥50% had members with ≤5 symptoms, it was designated a 'low symptom unit'. Five symptoms was selected as the cutpoint because it corresponded to approximately the median number of symptoms reported by both cohorts on the HSC (51% of the Devens cohort and 45% of the New Orleans cohort reported >5 symptoms). Another set of strata consisted of high and low symptom individuals (again using five symptoms as the cutpoint). The two stratifications together produced separate 2 × 2 tables (high/low units by high/low individuals) for both cohorts. Further stratification by gender was done (yielding eight cells). Approximately equal numbers of subjects were randomly selected from each to form the Devens and New Orleans target groups for this study.

The sampling lists were kept separate from the study data files. For recruitment, tracking, and testing, only the list of subject identification numbers was distributed. Thus, everyone on both the Boston-based and New Orleans-based research teams was blind to 'high/low' status during all phases of recruitment, testing, and interviewing. Only after data were entered into the computer was group status revealed.

Study protocol and measures

The complete study protocol included medical and occupational history questionnaires; several psychometric scales to assess psychological symptomatology (e.g. Brief Symptom Interview (BSI),[26] an environmental interview; a neuropsychological test battery; and psychological diagnostic interviews (including the Clinician Administered Scale for PTSD (CAPS).[27] The Institutional Review Board approved the protocol, and informed consent was obtained from the 343 subjects who participated (Devens

n = 220; New Orleans n = 73; Germany n = 50). A total of 300 subjects from the three study groups completed the questionnaires (Devens n = 186; New Orleans n = 66; Germany n = 48); 332 subjects (Devens n = 213; New Orleans n = 71; Germany n = 48) completed the environmental interview; and 254 subjects (Devens n = 148; New Orleans n = 58; Germany n = 48) subjects completed the in-person neuropsychological testing and psychiatric diagnostic interviews.

This report focuses on self-reported health symptoms and exposures reported by the participants who completed the 52-item Expanded Health Symptom Checklist and the environmental exposure section of the questionnaire.

Expanded Health Symptom Checklist

On the questionnaire each subject was asked to report the frequency that he/she experienced a specified set of health symptoms over the prior 30 days. Each health symptom response from a 52-item Expanded Health Symptom Checklist (HSC) was scaled from 0 to 4 (0 = no symptom; 1 = rarely, 1–2 times in all; 2 = some, 1–2 times/week; 3 = often, several times/week; 4 = very often, almost every day). Reporting the symptom at least once a week (score of 2, 3, or 4) was considered endorsement of a symptom.

Each of the 52 symptoms was assigned to one of nine different body systems by four independent judges, and agreement by at least three of four judges was required to classify a symptom. The judges were an occupational health physician, an environmental health specialist, an environmental epidemiologist, and a neuropsychologist. The nine body systems were cardiac; dermatological; gastrointestinal; genitourinary; musculoskeletal; neurological; neuropsychological; psychological; and pulmonary (c.f. Table 2 for symptoms assigned to each). In cases where more than three symptoms were classified in a specific body system, the three most representative symptoms were chosen by consensus of the judges. Body-system symptom (BSS) scores were the sum of the ordinal symptom frequency scale (0–4) for symptoms in each system.

Environmental exposures

Gulf-deployed subjects were asked to record on the questionnaire whether they were exposed to several Gulf-specific exposures, including anti-nerve gas pills, pesticides, debris from Scuds, smoke from burning oil wells, vehicle exhaust, smoke from tent heaters, and smoke from burning human waste. Each exposure response was scaled 0 to 2 (0 = no exposure; 1 = exposed; 2 = exposed and felt sick at the time). In addition, we examined item #17 from the Expanded Combat Exposure Scale (see below) which asked the frequency of exposure to poison gas or germ warfare (0 = none, 1 = once, 2 = ⩾2 times), referred to as 'CBW agents' in the analyses. We evaluated a binary yes/no response (0 = no, 1 or 2 recoded to 1 = yes) for each of these eight exposure variables.

Post-traumatic stress disorder and war-zone exposure

A clinical diagnosis of PTSD (dichotomous outcome) was determined using the CAPS for 75% of the subjects; continuous scores which measured PTSD symptomatology from the Mississippi Scale for Desert Storm War Zone Personnel (adapted from Keane *et al.*[28]) were determined for 99% of the study subjects. Subjects were categorized as having PTSD (1) if diagnosed with current PTSD on the CAPS, or (2) if the Mississippi PTSD score was >89 in subjects for those who did not complete the CAPS. This cutoff has previously been used to screen for wartime PTSD in community-based Vietnam-era veterans.[15] Data from subjects who had both CAPS and Mississippi measures showed that using a cutoff of 89 resulted in 73% sensitivity and 87% specificity in this population.

The Expanded Combat Exposure Scale (CES) is a 34-item scale designed to assess the presence and frequency of a range of prominent war-zone stressors, and *a priori* scoring protocols yield two summary scores: the traditional scale (Laufer) score 29 (score range: 0–14), and the Expanded scale score 30 (score range: 0–32). The latter score includes, in addition to traditional combat experiences, exposures to specific events encountered during PGW service (e.g. lack of communication among units, exposure to poison gas or germ warfare, placement on formal alert for chemical or biological warfare attack). In our data, the Expanded CES score was found to relate more strongly to increased symptom reporting; thus, that summary score was used in the analyses.

Analyses

Descriptive characteristics between the study groups were compared (unweighted analyses). Prevalence rates of individual symptoms were compared among the Devens, New Orleans, and Germany cohorts. Since women were oversampled and Gulf-deployed subjects reporting higher numbers of symptoms on the earlier surveys were more likely to participate, weighted analyses were performed using the SUDAAN statistical analysis package[31] to account for the sampling design and increased participation by subjects who report more symptoms on earlier survey. To ensure that differences between cohorts are not due to demographic differences, adjusted symptom prevalence rates are presented for each cohort, controlling for age, sex, and education through logistic regression. Odds ratios (OR) and 95% confidence intervals (CI) were computed from the logistic regression models.

The three study groups were also compared across individual BSS scores. Because the distributions of the scores were skewed (with a large proportion of subjects with scores near zero and a smaller proportion of subjects with very high scores), scores were log transformed for analysis. Mean BSS scores were compared across the three study groups through analysis of covariance (controlling for age, sex, and education level) using SUDAAN to account for sampling factors and participation bias.

The Devens and New Orleans cohorts were combined to explore associations between various self-reported Gulf War exposures and the log transformed BSS scores. A series of multiple regression analyses were run to explore the relationships between self-reported exposures and body-system symptomatology, controlling for age, sex, education, study site (Devens or New Orleans), PTSD status, and the Expanded CES score. First, a series of regressions individually examined each of the hypothesized exposure-symptom group relationships. Second, all exposures significantly related to a BSS score in the prior regression analyses were included in a regression model for each BSS score to account for correlation between exposures and thus ascertain if key exposures could be identified. To additionally examine the effect of traumatic stress on the hypothesized exposure-effect relationships, these two types of regression analyses were also performed excluding subjects with

PTSD. To explore the effect of depressive symptomatology, the first series of regression analyses were rerun adding the BSI subscale score for depression to the models. As the regression analyses were not focused on estimating overall prevalence rates, and sex was included as a covariate, they were performed using the SPSS statistical system[32] and thus, were not weighted for sampling factors. Results from the regression analyses are described by presenting the standardized regression coefficients (β) for the exposure of interest, for an easier comparison between exposure effects.

Results

Participation

The Devens cohort has been under study since 1991, and thus allows some assessment of possible bias concerning participation in the study. The 186 Devens subjects who completed the questionnaires differed from the 353 target subjects in the sample frame in that they were more likely to be female, white, older, better educated, and to have reported >5 symptoms on the 1992/1993 survey than we would expect from the stratified random sampling. They did not differ in employment status, marital status, alcohol or drug use, or military service status (as assessed at the 1992/1993 survey). Similarly, the New Orleans cohort participants were more likely to be female and to have reported >5 symptoms on the initial survey. Thus, weighting for the oversampling of females and participation bias was taken into account in the analyses comparing symptom rates across study groups.

Symptom change over time

Because the 20 health symptoms in the Health Symptom Checklist, administered to the Devens cohort in 1992/1993 and at the initial survey of the New Orleans cohort, were a subset of the 52-item Expanded HSC administered in this study, a comparison across the two survey points was done to see if there was a significant increase in health symptom reporting over time. No significant increase over the 2–4 year time period was noted for either the Devens or New Orleans groups. The mean number of symptoms reported by the 186 Devens subjects was 7.3 (SD = 4.9), whereas the mean number reported by these same individuals in 1992/1993 was 7.1 (SD = 4.9; Student's t-statistic for paired samples = 0.35, $P = 0.72$, correlation coefficient = 0.57). For the 66 New Orleans subjects, the mean number of symptoms in the current study was 6.7 (SD = 5.0), whereas the mean reported by these same individuals at the earlier time point was 7.1 (SD = 5.0; Student's t-statistic for paired samples = –0.58, $P = 0.57$, correlation coefficient = 0.39). Few significant differences were noted (McNemar's test) when endorsement of the individual symptoms was compared between the two time points.

Demographic comparison of the groups

Crude (unweighted) comparisons of the Devens and New Orleans groups revealed no significant differences in age, education level, sex, employment, prior Vietnam service, marital status, or Expanded CES score (Table 1) in the current study. There were differences in race, current duty status, smoking status, and level of PTSD symptomatology. Compared to the Gulf-deployed groups, the Germany-deployed group was older and had a larger proportion of males, and by its nature, consisted mostly of National Guard members.

On weighted analyses (accounting for the oversampling of females and participation bias), the three study groups were compared for certain demographic characteristics and observed to differ significantly on sex and age, but not education level. The New Orleans group had a significantly higher percentage of females (21%) than the Devens (10%) or Germany (14%) groups. The Germany group had a significantly higher mean age (41.0 years) than the Devens (36.2 years) or New Orleans (35.4 years) groups.

Post-traumatic stress disorder rates

Approximately 5% (8/148) of the Devens group, 7% (4/58) of the New Orleans group, and none of the Germany group were diagnosed with current PTSD on the CAPS. The rates of PTSD (including those subjects who did not complete the CAPS but had a Mississippi score >89) in the Gulf-deployed groups averaged 8.0% (8.1% for Devens; 7.6% for New Orleans). Those subjects with PTSD had significantly higher Expanded CES scores (11.1 versus 6.3 for subjects without PTSD, $P = 0.001$).

Comparison of health status

Both the Devens and New Orleans groups reported significantly poorer ratings of health and functional status (on the MOS Short Form-36[33]) than the Germany group.

A comparison of the three study groups (after adjusting for the oversampling of females, participation bias, and age, sex, and education differences) on the prevalence rates for the 24 individual symptoms which make up the BSS scores is presented in Table 2. Overall, both Gulf-deployed groups reported higher individual symptom prevalences compared to the Germany-deployed group on all but one of the 52 symptoms ('excessive sweating', where the Germany-deployed group reported a higher rate than the New Orleans group). The Devens group reported significantly higher symptom rates than the Germany group for 35 of 52 symptoms; the New Orleans group reported significantly higher symptom prevalence than the Germany-deployed group for 24 of 52 symptoms. Differences between symptom prevalences in the Devens and New Orleans groups were significant for only two of 52 symptoms ('excessive sweating', 'hallucinations'). The three most prevalent symptoms endorsed by the Devens and the New Orleans groups were 'forgetfulness', 'fatigue or easily tired', and 'restless or unsatisfying sleep'. The three most prevalent symptoms endorsed by the Germany-deployed group were 'awaken earlier than desired', 'forgetfulness', and 'backaches'.

Mean BSS scores were higher for both Gulf-deployed groups than the Germany-deployed group, with the Devens group reporting significantly higher scores (more frequent symptoms) for eight of the nine system scores (with genitourinary system symptoms being the exception) and the New Orleans group reporting significantly higher scores for six of the nine systems (with genitourinary, pulmonary, and cardiac system symptoms being the exceptions). There were no significant differences in mean BSS scores between the Devens and New Orleans groups.

When those people with PTSD were removed from the analyses, the Persian Gulf-deployed groups still report significantly higher individual symptom prevalences and BSS scores compared to the Germany group.

Table 1 Descriptive characteristics and comparisons (unweighted) between study groups

	Gulf-deployed		Germany deployed (G)	Comparison of groups[a]		
	Devens (D) (n = 186)	New Orleans (NO) (n = 66)	(n = 48)	(D:G)	(NO:G)	(D:NO)
Age (SD)[b]	34.7 (9.3)	34.3 (8.8)	41.0 (9.0)	<0.001	<0.001	ns
Education (SD)	13.9 (2.2)	4.2 (2.0)	3.7 (1.5)	ns	ns	ns
War-zone exposure						
Laufer score (SD)	3.3 (2.2)	2.9 (2.4)	not asked	–	–	ns
Expanded CES score (SD)	6.9 (4.4)	5.8 (4.5)	not asked	–	–	ns
Mississippi PTSD Scale 35-item score (SD)	72.3 (22.1)	79.3 (10.7)	57.3 (11.8)	<0.001	<0.001	0.001
% Female	46.2	48.5	14.6	<0.001	<0.001	ns
% Caucasian	90.8	53.0	100.0	0.03	<0.001	<0.001
% Unemployed	12.3	16.7	14.6	ns	ns	ns
% Married	54.3	52.3	74.5	0.01	0.02	ns
% Vietnam service	11.4	13.6	41.7	<0.001	0.001	ns
Current duty status						
% Active	2.8	1.5	0.0	ns	ns	ns
% Reserve	24.3	43.9	6.3	0.005	<0.001	0.003
% Guard	30.9	24.2	70.8	<0.001	0.001	ns
% Civilian	34.8	24.3	18.8	0.04	ns	ns
% Right-handed	86.0	89.4	85.4	ns	ns	ns
% Repeated grade in school	22.2	15.4	22.9	ns	ns	ns
% Reported alcohol problem	7.9	16.1	6.7	ns	ns	ns
% Ever taken non-prescription,psychotropic drugs	9.7	4.6	8.3	ns	ns	ns
% Ever taken sedatives	10.9	15.6	10.4	ns	ns	ns
Smoking status						
% non-smoker	43.0	60.0	43.8	ns	ns	0.02
% ex-smoker	27.4	13.8	27.1	ns	0.09	0.03
% current smoker	29.6	26.2	29.2	ns	ns	ns
General health: % reported fair or poor	20.7	19.7	6.4	0.03	0.06	ns
Current health: (versus one year ago)						
% worse or somewhat worse	28.6	27.3	6.4	0.001	0.006	ns

[a] Student's t-test was used for comparisons of differences in mean scores for continuous variables.

[b] SD = standard deviation.

χ^2 statistic was used for comparison of differences in proportions for categorical variables.

ns = not significant, $P > 0.10$.

Environmental exposures and symptoms

All of the Gulf-deployed subjects in this study were deployed to the Iraq, Saudi Arabia, and/or Kuwait areas of the Southwest Asia theatre of operations. The majority of the Devens and New Orleans subjects reported exposure to a number of the potential environmental risks (Table 3). For the eight exposures, six subjects failed to report at least one of these exposures, and 59% of the subjects reported five or more exposures.

The first set of multiple regression analyses of the associations between the individual environmental exposures and BSS scores (with age, sex, education, study site, Expanded CES score and PTSD status as covariates) produced significant relationships for each exposure and scores of the predicted BSS groupings (Table 4), with the exception of exposure to smoke from oil fires and exposure to anti-nerve gas pills, neither of which was significantly related to the predicted body system symptoms. Self-reported exposure to pesticides, debris from Scuds, CBW agents, and smoke from tent heaters were each consistently related to hypothesized BSS scores, with standardized regression coefficients ($\beta = 0.15$–0.28).

Among the covariates, PTSD status was significantly related to all BSS scores ($P < 0.05$), with standardized regression coefficients ranging from 0.16 (for musculoskeletal symptoms) to 0.28 (for neuropsychological symptoms). Cardiac, gastrointestinal, and neurological symptom scores were higher for females; those with lower education had higher neuropsychological and pulmonary scores. War-zone exposure (Expanded CES score) was only significantly related to higher dermatological scores. Study site was not related to any of the BSS scores in these models.

A second set of multiple regression analyses (with all covariates) was performed with all the significant exposures as identified in Table 4 entered as independent variables in order to examine whether key exposures could be identified for each of the BSS scores. The cardiac symptom score was associated with exposure to smoke from tent heaters ($\beta = 0.20$, $P = 0.011$), while exposure to vehicle exhaust or smoke from burning

Table 2 Prevalence rates (%) of health symptoms[a]

	Gulf-deployed		Germany deployed	Odds ratios[b]
	Devens (n = 186)	New Orleans (n = 66)	(n = 48)	(Devens, New Orleans)
Cardiac				
Irregular heart beats or 'heart flutters'	7.1	4.4	1.8	4.1, 2.4
Chest pain	6.0	2.9	0.0	–
Racing heart	5.2	3.3	1.8	3.0, 1.8
Dermatological				
Skin rashes, eczema, skin allergies	15.5	11.7	1.9	9.6,[c] 6.9[c]
Gastrointestinal				
Stomach cramps or excessive gas	23.1	18.0	3.6	8.0,[c] 5.8[c]
Diarrhoea or constipation	19.3	13.6	3.9	5.9,[c] 3.9
Nausea and/or upset stomach	16.9	19.3	0.2	–
Genitourinary				
Frequent urination (passing water)	11.1	5.6	5.5	2.2, 1.0
Pain during intercourse	2.4	1.9	0.0	–
Musculoskeletal				
Joint pains	33.0	31.5	16.0	2.6,[c] 2.4
Backaches	27.9	33.2	18.3	1.7, 2.2
Neckaches or stiffness	25.0	18.0	10.9	2.7,[c] 1.8
Neurological				
Headaches	30.8	31.3	9.6	4.2,[c] 4.2[c]
Numbness in arms/legs	14.9	14.9	5.8	2.8, 2.8
Dizziness or feeling lightheaded	11.5	11.1	2.0	6.4, 6.2
Neuropsychological				
Difficulties learning new material	9.3	7.3	1.3	7.9,[c] 6.0
Difficulty concentrating	33.7	29.6	7.4	6.4,[c] 5.2[c]
Confusion	5.7	4.5	0.1	–
Psychological				
Inability to fall asleep	29.6	30.9	11.0	3.4,[c] 3.6[c]
Frequent periods of feeling depressed	22.6	5.8	4.6	6.0,[c] 3.9
Frequent periods of anxiety or nervousness	17.8	14.0	3.0	7.1,[c] 5.3[c]
Pulmonary				
Difficulty breathing or shortness of breath	13.5	10.9	4.1	3.6, 2.8
Common cold or flu	10.8	6.4	0.1	–
Rapid breathing	4.4	3.4	2.1	2.1, 1.6

[a] The estimated prevalence rates represent the expected symptom rates in the larger 1992/1993 cohort from Devens, the initial cohort from New Orleans, and the overall Germany-deployed unit from Maine.

[b] All comparisons are weighted for sampling design, participation bias, and adjusted for age, sex and education using SUDAAN.

[c] 95% confidence interval excludes 1.0.

– Odds ratios cannot be calculated because the rate in the reference group (Germany) is 0 (or it is not meaningful as the rate is <0.5).

Table 3 Frequency (% yes) of self-reported environmental exposures in the Persian Gulf-deployed groups

Exposure variable	Devens	New Orleans
Anti-nerve gas pills	66.6%	77.0%
Pesticides	49.1	27.3
Debris from Scuds	51.7	43.1
Chemical or biological warfare (CBW) agents	23.9	14.8
Smoke from burning oil wells	84.9	72.3
Vehicle exhaust	90.3	86.4
Smoke from tent heaters	69.8	50.0
Smoke from burning human waste	75.3	50.8

human waste was no longer significant. For the musculoskeletal score, exposure to CBW agents ($\beta = 0.18$, $P = 0.015$) and exposure to pesticides ($\beta = 0.19$, $P = 0.011$) remained significant while exposure to debris from Scuds was no longer significant. For the neurological, neuropsychological, and psychological scores, both debris from Scuds ($\beta = 0.18$–0.19) and CBW agents ($\beta = 0.15$–0.19) remained significant. For the pulmonary score, smoke from tent heaters remained significant ($\beta = 0.21$, $P = 0.007$).

When people who met the criteria for PTSD were removed from the analyses (resulting in lower sample size) most of the associations between individual exposures and BSS scores,

as described above, were essentially unchanged: self-reported exposure to smoke from tent heaters remained significantly related to cardiac, neurological, and pulmonary scores ($\beta = 0.27$, 0.21, 0.24, respectively); vehicle exhaust was significantly related to cardiac and neurological scores ($\beta = 0.14$ and 0.17, respectively); smoke from burning human waste was significantly related to cardiac and pulmonary scores ($\beta = 0.22$ and 0.16, respectively); debris from Scuds was significantly related to musculoskeletal, neurological, neuropsychological, and psychological scores (β ranging from 0.19 to 0.25); exposure to CBW agents remained significantly related to musculoskeletal, neuropsychological, and psychological scores ($\beta = 0.18$, 0.18, and 0.21 respectively); and pesticide exposure was significantly related to musculoskeletal and neurological scores ($\beta = 0.25$ and 0.15, respectively). Analyses to identify key exposures resulted in the same findings as in the prior analyses with PTSD subjects included, except that exposure to CBW agents were only of borderline significance for neurological ($\beta = 0.13$, $P = 0.089$) and musculoskeletal ($\beta = 0.13$, $P = 0.093$) scores.

The overall significance patterns between exposures and hypothesized BSS scores (Table 4) did not change when the BSI subscale score for depression was added to the regression models: self-reported exposure to pesticides, debris from Scuds, CBW agents, and smoke from tent heaters remained significantly associated ($P < 0.05$) with the BSS scores. The exceptions were that exposure to CBW agents was no longer significantly related to neurological and neuropsychological body system scores ($P > 0.05$). Self-reported exposure to debris from Scuds and vehicle exhaust were each then marginally associated ($P = 0.06$) with musculoskeletal and neurological body system scores, respectively. When the depressive symptomatology indicator score was added to the models exploring the effect of exposure to anti-nerve gas pills, the relationships between this exposure and the musculoskeletal ($\beta = 0.16$) and neuropsychological ($\beta = 0.13$) scores were significant.

Discussion

The subject groups evaluated in this study were selected from larger cohorts being followed longitudinally, and a unique comparison group (people deployed to a foreign location other than the Gulf during the time of the PGW) has been included. Although the study sample has a higher proportion of Army Reserve and National Guard troops compared to that of the total US Gulf force, this study permits evaluation of health symptoms over a more representative sample of PGW veterans with respect to military branch, unit status, and occupational status within unit than other recent studies[3,5,34–36] of specific units and self-selected volunteer participants. Results from the Iowa study[37] suggest that there may be some differences in the level of certain symptoms reported by Reserve and Guard members compared to Active duty troops deployed to the Gulf. However, to date, no studies have systematically examined possible patterns to or sources of these differences. Gulf Reserve and Guard troops may have had some specific environmental exposures that were different from the Active duty forces. Also, Reserve and Guard troops were older and probably had different preparation for combat-related activities.

Examination of individual environmental exposures and their relationships to specific body system symptom groupings reveals that several self-reported Gulf exposures are associated with increased reporting of outcomes predicted prior to

Table 4 Standardized regression coefficients (and *P*-values) describing the relationship between exposures and body system symptom scores[a]

	Body system symptom groups							
Exposures	Cardiac	Dermatological	Gastro-intestinal	Musculo-skeletal	Neurological	Neuro-psychological	Psychological	Pulmonary
Anti-nerve gas pills			0.04 (ns)	0.13 (ns)	0.06 (ns)	0.10 (ns)	0.03 (ns)	
Pesticides[b]		0.03 (ns)	0.12 (ns)	0.25 (0.001)	0.18 (0.007)	0.12 (ns)	0.11 (ns)	
Debris from Scuds		0.01 (ns)		0.17 (0.017)	0.26 (<0.001)	0.21 (0.001)	0.22 (0.001)	
CBW agents[b]		0.09 (ns)		0.24 (0.001)	0.18 (0.013)	0.18 (0.009)	0.23 (0.001)	
Smoke—oil fires	0.0 (ns)				0.11 (ns)			0.10 (ns)
Vehicle exhaust	0.15 (0.026)				0.15 (0.024)			0.12 (ns)
Smoke—tent heaters	0.28 (<0.001)				0.22 (0.001)			0.25 (<0.001)
Smoke—burning human waste	0.23 (0.001)				0.12 (ns)			0.17 (0.015)

[a] From multiple regression model with log body system symptom scores as dependent variables; age, education, gender, study site, PTSD status, and war-zone (Expanded CES score) exposure as covariates; individual hypothesized exposures as independent variables.

[b] Both pesticides and CBW agents had a higher number of unknown or non-responses. For these two variables, the unknown group was coded as an exposure category in the analyses; effects reported are for the differences between those who responded as having been 'exposed' and those who responded 'unexposed'.

(ns) = not significant, $P > 0.05$.

analyses. Analyses to identify key exposures found self-reported exposure to smoke from tent heaters was significantly associated with both cardiac and pulmonary scores; self-reported exposure to pesticides and CBW agents were significantly associated with musculoskeletal scores; and self-reported exposures to debris from Scuds and CBW agents were significantly associated with neurological, neuropsychological, and psychological scores. No significant associations of exposures with hypothesized gastrointestinal or dermatological symptom scores were observed.

These results were obtained after controlling for the impact of war-zone stressors and PTSD status, as well as the effects of age, sex, education, and study site, thus suggesting that traumatic stress is not the sole explanation for increased health symptom reporting in Gulf War veterans. As an additional check, environmental exposures were associated with increased health symptom reporting when subjects with PTSD were excluded from the analyses.

Interpreting the role of traumatic stress in studies of veterans' health is complicated by the fact that stress as a variable is measured both as exposure to a stressor event and also in terms of how specific events affect the subject through physiological symptomatology (an outcome). Thus, stress operates as a potential confounder in any assessment of the relationship between wartime environmental exposures and health effects. Some have been critical of published reports of PTSD in PGW veterans that rely on the Mississippi PTSD scale score as an indicator,[38] as this score may not by itself specifically measure PTSD but include comorbid symptomatology (e.g. depression, anxiety, cognitive difficulties). By including both PTSD status (primarily assessed with clinical diagnostic methods) and war-zone exposure score in the regression models in this paper, the analytical design may have overcontrolled for the potential effect of traumatic stress on the exposure-health relationships under study. Thus, the results described represent a conservative interpretation of the data.

The primary focus of this paper is the effect of self-reported Gulf-service exposures on health symptomatology, controlling for traumatic stress as a possible explanation. Besides traumatic stress, the role of clinical depression and depressive symptomatology or adjustment difficulties may result in reports of poorer health status. However, the converse is also true; poorer health status may result in increased depressive symptomatology. In addition, certain neurotoxicant exposures may produce depressive symptomatology.[39] It is difficult to tease out these cause and effect relationships in an observational study. In the primary analyses, depressive symptomatology was not included as a covariate due to the concern that because it may be the result (outcome) of neurotoxicant exposure, we would be overcontrolling for the effect of exposures on those types of health symptom complaints. However, when the regression analyses were re-run adding the BSI subscale score for depression (an indicator score of depressive symptomatology) to the models, the overall significance patterns between exposures and body system scores (BSS) depicted in Table 4 did not change: self-reported exposure to pesticides, debris from Scuds, CBW agents, and smoke from tent heaters remained significantly associated with the BSS scores. Only prospective studies can begin to adequately address the intricate causal relationships between toxicant exposures, health, and stress. Further analyses of the longitidinal data available for these study subjects to address the development of physical and psychological symptoms is planned.

In addition to the difficulty in intepretation of the causal relationships between exposure, health symptomatology, and stress within a cross-sectional study design, it is well recognized that there is high comorbidity between PTSD and clinical depression and depressive symptomatology.[40,41] In these cohorts, clinical diagnoses of PTSD and Major Depression are significantly correlated (correlation coefficient $r = 0.35$, $P < 0.001$), as are PTSD and general psychopathological symptomatology ($r = 0.39$, $P < 0.001$). The role of lower magnitude, non-traumatic stress on PGW veterans' health symptom reporting and the role of psychiatric comorbidity (e.g. clinical depression) are being examined in further studies.

The results confirm earlier studies[5,35,37,42] that have shown that health symptoms are endorsed at higher rates in Persian Gulf-deployed groups than in non-Gulf-deployed groups. It is interesting that the most prevalent symptoms are the same in the Gulf- and Germany-deployed groups, with the Gulf-deployed veterans simply reporting higher prevalence rates than the Germany-deployed veterans. Further evaluation of symptom patterns, self-reported and surrogate measures of Gulf-related exposures, and objective clinical test findings in representative PGW veteran cohorts are needed to determine if there is a specific 'Gulf War Syndrome'. The possibility remains open that veterans do not suffer from one syndrome but rather experience a variety of specific symptoms related to specific exposures. The findings suggest that health issues concerning PGW veterans encompass effects of multiple environmental exposures resulting in health outcomes in different body systems. Additive and synergistic effects among different environmental exposures and interactions between environmental exposures and stress or other influences are probable and deserve further study.

This paper describes results obtained from information collected through self-report methods. As such, a possible explanation could be attribution, that is, people who feel they are sick are more likely to report environmental exposures. Although this explanation cannot be ruled out completely, it is important to note that associations predicted by *a priori* hypotheses about known toxicant effects were observed. In the future, our plan is to investigate exposure-health outcome relationships with non-subjective outcome data (neuropsychological test performance, pulmonary function, brain imaging) and other types of exposure data (e.g. air modelling of exposures, individual troop location information) for the same study subjects. At this juncture it is not clear that any of these alternatives are superior to self-report.

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